REMARKS

Summary of Personal Interview with Examiner

Applicants thank the Examiner for the courtesy of the telephonic interview conducted on October 16, 2007 during which the foregoing amendments to the claims and the outstanding rejections were discussed.

Amendments to the Claims

Claims 1-18, 22-25 and 27 were under examination as of the issuance of the Office Action of January 26, 2007. By the current Amendments to Claims, claims 1, 14 and 17 have been amended, new claim 28 has been added and claims 22-25 have been cancelled, without prejudice.

Support for the amendments to the claims and the introduction of the new claims can be found throughout the specification and in the claims as originally filed. Specifically, support for the amendment to claims 1, 14 and 17 can be found throughout the specification, for example, at page 6, lines 18-26 and the claims as originally filed, for example, claims 8-10. Support for new claim 28 can be found throughout the specification, for example, at page 8, lines 1-3.

No new matter has been added by the foregoing amendments or the introduction of a new claim. Applicants respectfully request that the aforementioned amendments be entered. Applicants note that the foregoing amendments and cancellation of claims have been made solely in order to expedite examination and should in no way be construed as an acquiescence to the validity of the rejections set forth in the Office Action. Following entry of the foregoing amendments, claims 1-18 and 27-28 will be pending.

Priority

Applicants confirm that a certified copy of the foreign Great Britain patent application will be filed shortly and certainly prior to the issuance of a patent based on the above-identified patent application.

Rejection of Claims 1-18, 22-25, 27 and 28 under 35 U.S.C. § 103(a)

Claims 1-18, 22-25, 27 and 28 have been rejected as being unpatentable over Dumont *et al.* (USPN 6,413,974) (hereinafter referred to as "the '974 patent") in view of Dumont *et al.* (USPN 6,399,633) (hereinafter referred to as "the '633 patent") and Carlson *et al.* (*Cancer Res.* (1999) 59:4634-4641) (hereinafter referred to as "Carlson") on the ground that

> [t]he Dumont et al. (US 6,399,633) reference was used to show that cyclin dependent kinase (cdk) inhibitors are used to monitor the levels of phosphorylated Rb and levels of phosphorylated erk1 and erk2. The instant claims are drawn to the method of monitoring the activity of roscovitine (a cdk2 and cdk4 inhibitor) and detecting the presence of phosphorylated erk1 and erk2 and not to the method of phosphorylating erk1 and erk2 via administration of roscovitine. Applicant asserts that roscovitine uniquely induces the phosphorylation of erk1 and erk2 but unique properties of compounds do not impart patentability, whereas the property is inherent to the compound. Also, only a property of the compound and not a specific method step, such as detecting the phosphorylation of erk1 and erk2 can be used to distinguish over the prior art. Dumont et al. (U.S. 6,399,633) explicitly discloses that the levels of phosphorylated Erk1 and Erk2 were measured upon administration of flavopiridol, a cdk2 and cdk4 inhibitor, with the phosphorylation-specific antibody... The method step of detecting the presence of phosphorylated erk1 and erk2 may reveal that there may be no phosphorylated erk1 and erk2 present. Although the disclosure reveals that the cdk inhibitor, flavopiridol, has not [sic] effect on MAP kinase phosphorylation, the method of monitoring the phosphorylation of Erk1 and Erk2 is clearly stated...
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> The combination of the references encompsses the instant claims where it would be obvious for one ordinarily skilled in the art to employ the ckd2[*sic*] and cdk4 inhibitor roscovitine as a cdk inhibitor equivalent/substitute to detect the presence of phosphorylated erk1 and/or erk2. Also, it is unnecessary for the examiner to provide for the expectation that roscovitine would induce phosphorylation of erk1 and erk2 as obviousness does not require absolute predictability.

Applicants respectfully disagree for the reasons of record. Notwithstanding the foregoing, solely in the interest of expediting examination and in no way acquiescing to the validity of the outstanding rejection, Applicants have amended claims 1, 14 and 17 to specify that an increase in erk1 and/ or erk2 phosphorylation is indicative of roscovitine or candidate drug activity.

Applicants submit that the teachings of the '633 patent teach away from the present invention. At least for this particular reason, the '633 patent, in view of the cited references and the state of the art, fails to undermine the nonobviousness of the pending claims. Specifically,

Applicants submit that the ***'633 patent teaches that flavopiridol fails to affect the phosphorylation of Erk1 and Erk2***, and as such, a skilled artisan would conclude that monitoring the phosphorylation of Erk1 and Erk2 can not be used to assess ***flavopiridol*** activity. Moreover, there is ***no evidence provided that one skilled in the art would believe that roscovitine, a CDKI, would act differently from flavopiridol, another CDKI,*** in this regard. As such, the '633 patent ***teaches away*** (as set forth in MPEP § 2145(X)(D)(2)) from such modification in suggesting that the class of CDKI's does not affect the levels of phosphorylation of Erk1 and Erk2 and, therefore, can not serve as pharmacodynamic markers to assess CDKI activity.

Indeed, the present invention is based on the ***unexpected finding that despite flavopiridol's failure to affect Erk1 and/ or Erk2 phosphorylation, another CKDI, i.e., roscovitine, does, in fact, affect Erk1 and/ or Erk2 phosphorylation.*** Accordingly, although the Examiner argues that "Applicant asserts that roscovitine uniquely induces the phosphorylation of erk1 and erk2 but unique properties of compounds do not impart patentability, whereas the property is inherent to the compound," Applicants submit that in assessing obviousness, the uniqueness of a property within a class of compounds is particularly relevant. For example, unique properties are relevant to the unexpectedness of Applicants' invention, particularly when the unique property contradicts the knowledge in the art that would otherwise lead a skilled artisan away from the claimed invention. Applying such standard to the present application, Applicants submit that one skilled in the art would not reasonably conclude that where a member (*i.e.*, flavopiridol) of a class of compounds (*i.e.*, CDKI's) does not exhibit a property (*i.e.*, phosphorylation of Erk1 and Erk2), that another member (*i.e.*, roscovitine) of the class would exhibit such property.

Applicants further submit that the '974 patent and Carlson each fail to account for the deficiencies of the '633 patent in this regard. Indeed, the '974 patent and Carlson each fail to resolve the '633 patents' teaching away from the present invention. Moreover, while the Examiner asserts that Carlson discusses RB phosphorylation, Applicants submit that the present claims are not directed to RB phosphorylation *per se* and that neither the '974 patent or Carlson even discuss CDKI's in the context of erk1 and erk2.

In summary, the Examiner's prima facie case of obviousness is predicated on the assumption that one skilled in the art would conclude that roscovitine activity ***can be*** monitored by assessing

Erk1 and Erk2 levels based on the knowledge that (1) flavopiridol activity ***can not be*** monitored by assessing Erk1 and Erk2 phosphorylation levels because flavopiridol ***does not affect*** phosphorylation of Erk1 and Erk2 and (2) roscovitine and flavopiridol are both CDKI's. Clearly, such conclusion is counterintuitive and, therefore, nonobvious, based on the facts presented by the Examiner. Indeed, one skilled in the art would not arrive at the claimed invention based on the teachings of the cited references and the state of the art.

Accordingly, because the prior art teaches away from the claimed invention and, further, because the claimed invention is unexpected in view of the state of the art at the time of the invention, Applicants submit that the claimed invention is nonobvious over the cited references and respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

Applicants believe that no additional fee is due with this submission. However, if the Applicants are in error, the Commissioner is authorized to charge any deficiency in the fees paid herewith, or credit any overpayment, to Deposit Account No. 12-0080, under Order No. CCI-026USRCE, from which the undersigned is authorized to withdraw.

If there are any remaining issues or if the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

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Respectfully submitted,

By /Maneesh Gulati/

Maneesh Gulati, Esq.
Registration No.: 60,963
LAHIVE & COCKFIELD, LLP
One Post Office Square
Boston, Massachusetts 02109
(617) 227-7400
(617) 742-4214 (Fax)
Attorney/Agent For Applicants